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Standard Pharmacist Intervention Checklist to Improve the Appropriate Use of Medications for Inpatients with Polypharmacy

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Inappropriate polypharmacy increases the risks of adverse drug reactions and hospitalization. Thus, it is important to evaluate the appropriateness of prescriptions in polypharmacy. We designed a checklist based on previous studies and guidelines for pharmacists in our hospital to evaluate the appropriateness of a prescription of multiple medications. The efficacy of checklist-based standardization was evaluated by investigating inpatient medical records and prescriptions. We designed a checklist for pharmacists in our hospital to evaluate the appropriateness of a prescription and reduce the prescription of medications with multiple administrations for all age groups. When patients using more than six medications were admitted, pharmacists assessed the prescriptions of these patients using the checklist. We examined 729 inpatients over the course of 4 months before and after the standardization. The research protocol was approved by the Human Ethical Committee of Showa University, School of Pharmacy. For prescriptions with six or more medications, the total number of suggestions for all patients significantly increased upon implementation of the checklist (50 vs. 21, $P < 0.05$). Additionally, the number of changes in prescriptions by doctors increased while using the checklist (44 vs. 17, $P < 0.05$), whereas the rate of changes per suggestions did not change. The most common reason for the increase in prescription suggestions after the standardization was a medication was prescribed to patients despite the absence of symptoms. Our checklist was effective in reducing the prescription of inappropriate medications in patients of all ages.

Key words polypharmacy, checklist, pharmacist, inpatient, inappropriate prescribing

INTRODUCTION

Polypharmacy is associated with various problems, and inappropriate polypharmacy increases the risks of adverse events[1-4] and ambulance-transported hospital admission.[5] In addition, complicated medication regimens are related to non-adherence.[6,7]

Multimorbidity is a major factor leading to polypharmacy. The prevalence of multimorbidity substantially increases with age, and most patients aged 65 years and older have multimorbidity.[8] As the rate of polypharmacy increases, the risk of potential drug interactions increases, and this is a clinical concern for patients.[9] The Beers' criteria, published in 1991, and the STOPP/START criteria, published in 2008, tools aimed to detect prescriptions of potentially inappropriate medications, are regularly revised.[10,11] In Japan, a similar guideline was introduced by The Japan Geriatrics Society in 2015.[12] Intervention trials to control polypharmacy in elderly patients using these criteria have reportedly reduced inappropriate prescriptions.[13,14]

The criteria was designed for elderly patients, focusing on potentially inappropriate medications for the elderly. Pharmacists must check whether the prescribed medications have precautions listed among the criteria. However, it is not easy to check each medication in the prescription against the criteria for every patient in the hospital. Polypharmacy is generally a condition of being prescribed six or more medications, although the most important issue of polypharmacy is the potential risk of inappropriate medication usage. As polypharmacy prescriptions are not limited to elderly patients, we designed a general checklist for the assessment of any prescription. Each item in the checklist is a basic question about the patient's conditions or a general evaluation of medications. Each point in the list was selected based on previous studies and guidelines.[12,15-20]

This checklist was introduced at our hospital in 2016. Since then, the pharmacists in our hospital have been using it to evaluate the appropriateness of prescriptions for medications with multiple administrations. In this study, we evaluated the efficacy of the standardization using patient medical records and prescription history.

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Table 1. Checklist for Pharmacists to Evaluate the Appropriateness of Prescriptions

1. Is there an unnecessary duplication of other medications?
2. Are there any symptoms for the medication prescribed?
3. Are there any adverse symptoms or signs that may be related to medications?
4. Is there an additional medication prescribed to treat adverse effects without noticing the adverse effects?
5. Are there clinically important drug–disease/condition interactions?
6. Is the dosage correct?
7. Are the directions correct?
8. Are there clinically important drug–drug interactions?
9. Is the duration of therapy acceptable?
10. Is there an indication for the medication?
11. Is the medication effective for the condition?
12. Does the patient adhere to his/her medication schedule?
13. Is there a less expensive alternative medication that is equally effective?
14. Are there medications in the prescription that should be discontinued for patients older than 75 years?

MATERIALS AND METHODS

Standardization of Prescription Confirmation Our checklist was designed to evaluate the appropriateness of a prescription based on the Medication Appropriateness Index[15] and the Guidelines for Medical Treatment and Its Safety in the Elderly 2015 from the Japan Geriatrics Society.[12] The items in the checklist were discussed and revised by pharmacists with more than 5 years of clinical experience, based on polypharmacy-related studies to reduce medications.[16-20]

Since May 2016, this checklist has been used in our hospital. When patients were admitted with more than six medications, ward-based pharmacists assessed the prescriptions of these patients using the checklist. Prescriptions that followed the recommendations of the package insert were defined as appropriate, and those that did not match the dosage and directions for administration were defined as inappropriate.

Patient Distribution This study was performed in our hospital from January to August 2016. The study involved inpatients in the Departments of Neurology; Diabetes, Metabolism, and Endocrinology; Rheumatology; and Clinical Immunology. The data of all patients were divided into two groups: before and after the introduction of the checklist. Patients participating in clinical trials and those who were not issued a discharge prescription were excluded.

The number of prescription medications at admission and discharge was examined using the medical records of patients. External medications, such as ointments and poultices, and as-needed medications were excluded from the medication counts. Patients were classified into two groups based on the number of prescription medications at admission: (i) five or fewer and (ii) six or more medications at admission. The patients were then classified into three groups: (i) $\leq$ 65 years old, (ii) 65-75 years old, and (iii) $\geq$ 75 years old.

Evaluation of Interventions for Polypharmacy by Pharmacists We counted the suggestions for prescriptions by pharmacists and the changes to prescriptions by doctors during the 4-month period before and after the standardization. Additionally, we examined the details of the medications that were removed from prescriptions. The information of patients was anonymously extracted from their medical records.

Statistical Analysis Fisher's exact test was used to compare the categorical variables. Results with a P-value of ≤ 0.05 were considered significant. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). It is a modified version of R commander designed to add statistical functions that are frequently used in biostatistics.[21]

Ethical Considerations The research protocol was approved by the Human Ethical Committee of Showa University, School of Pharmacy (approval number 261). This study did not require patient consent due to the anonymous nature of data extraction.

RESULTS

Standardization of the Confirmation of Prescriptions We designed a checklist for the pharmacists in our hospital to evaluate the appropriateness of prescriptions and reduce the number of medications prescribed for administration on multiple occasions (Table 1).

Distribution of Patients We examined the data of 729 hospitalized patients, of whom 378 and 351 were treated during the 4 months before and after the introduction of the checklist, respectively. Patients participating in clinical trials and those who had not been issued prescriptions were excluded (121 and 79 patients treated before and after the introduction of the checklist, respectively). The number of eligible patients in the before and after groups was 257 and 272, respectively. The patients in the chronological groups were divided into two groups based on the number of prescribed medications at admission. The number of patients prescribed six or more medications at admission in the before and after groups was 161 and 163, respectively (Fig. 1).

Table 2 shows the characteristics of the study population. There were no statistical differences in age, number of medications at admission, number of medications at discharge, or duration of hospitalization between the before and after groups. The number of patients who was added the medications in the before and after groups was 98 and 92, respective-

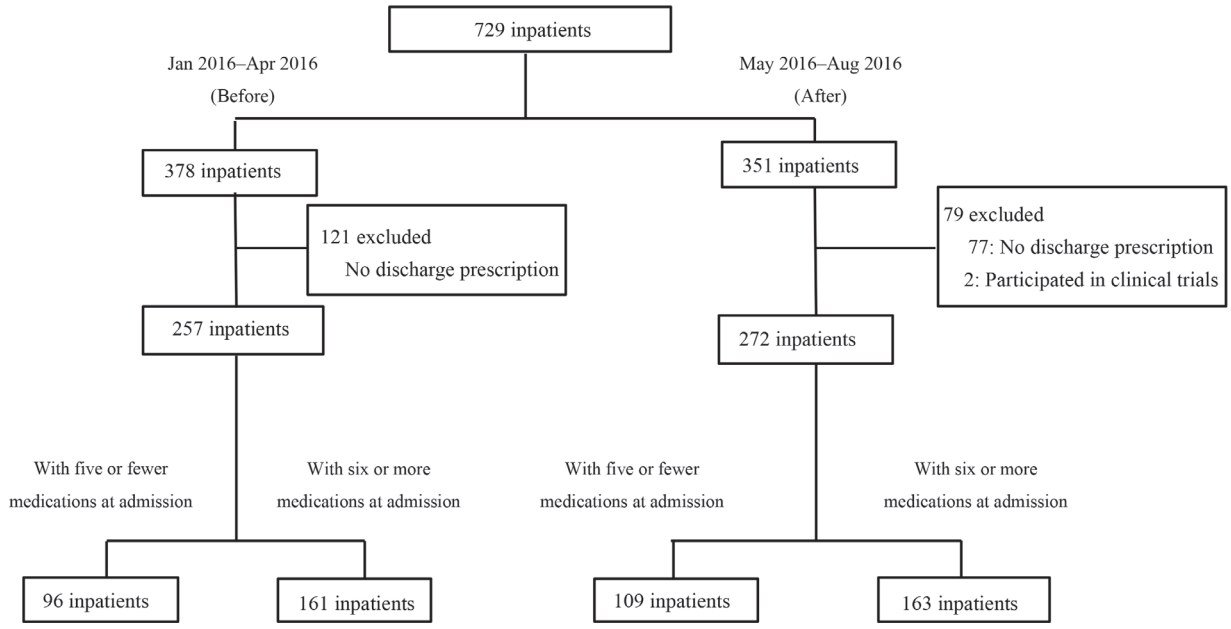

Fig. 1. Distribution of Patients

ly. The average number of increased medications in the before and after groups was 2.2 ± 1.8 and 2.1 ± 1.7, respectively.

Evaluation of Polypharmacy Intervention by Pharmacists Table 3 shows the number of suggestions for prescriptions by pharmacists and the number of changes made to prescriptions by doctors. The total number of suggestions for prescriptions with six or more medications was significantly higher after checklist introduction than before its introduction (50 vs. 21, $P < 0.05$). The number of suggestions increased in all age groups. We observed a statistically significant increase in the number of prescription suggestions only for patients aged ≥ 75 years, although the younger groups showed a similar increase. The total number of changes in prescriptions by doctors was significantly higher while using the checklist than before implementing the checklist (44 vs. 17, $P < 0.05$). There was a statistically significant difference in the number of changes in prescriptions for patients aged ≥ 75 years before and after using the checklist, but the differences between the other two age groups did not reach statistical significance. The percentage of suggestions that led the doctors to change prescriptions was approximately 80% to 90%, and it remained consistent before and during the use of the checklist. After intervention by pharmacists, there was no change in the conditions of patients during hospitalization.

Table 2. Patient Characteristics

Patients (n = 529)	Jan 2016-Apr 2016 (n = 257)	May 2016-Aug 2016 (n = 272)	*P*-value
Age†	68.5 ± 16.1	68.2 ± 16.4	0.827
No. of medications at admission†	7.4 ± 4.2	7.1 ± 4.3	0.398
< 6 medications‡	96 (37.4%)	109 (40.1%)	
≥ 6 medications‡	161 (62.6%)	163 (59.9%)	
Age < 65 years old‡	42 (26.1%)	37 (22.7%)	
Age 65-74 years old‡	35 (21.7%)	46 (28.2%)	
Age ≥ 75 years old‡	84 (52.2%)	80 (49.1%)	
No. of medications at discharge†	7.4 ± 3.7	6.9 ± 3.8	0.085
< 6 medications‡	86 (33.5%)	111 (40.8%)	
≥ 6 medications‡	171 (66.5%)	161 (59.2%)	
Age < 65 years old‡	47 (27.5%)	44 (27.3%)	
Age 65-74 years old‡	39 (22.8%)	40 (24.8%)	
Age ≥ 75 years old‡	85 (49.7%)	77 (47.8%)	
Duration of hospitalization (d)†	20.2 ± 18.2	20.6 ± 20.8	0.811

n: total number of patients
†The data are expressed as mean ± standard deviation.
‡The data are expressed as number of patients with percentages in parentheses.

Table 3. Numbers of Pharmacist Suggestions for Prescriptions and Changes Made to Prescriptions by Doctors

		Suggestions				Changes		
Age		Before	After	*P*-value		Before	After	*P*-value
		n = 161	n = 163			n = 161	n = 163	
All	Suggestions	21 (13.0%)	50 (30.7%)	<0.05	Changes	17† (10.6%)	44† (27.0%)	< 0.05
	No Suggestions	140 (87.0%)	113 (69.3%)		No Changes	144 (89.4%)	119 (73.0%)	
		n = 42	n = 37			n = 42	n = 37	
< 65	Suggestions	4 (9.5%)	8 (21.6%)	0.209	Changes	3 (7.1%)	7 (18.9%)	0.176
	No Suggestions	38 (90.5%)	29 (78.4%)		No Changes	39 (92.9%)	30 (81.1%)	
		n = 35	n = 46			n = 35	n = 46	
65-74	Suggestions	2 (5.7%)	10 (21.7%)	0.060	Changes	2 (5.7%)	9 (19.6%)	0.103
	No Suggestions	33 (94.3%)	36 (78.3%)		No Changes	33 (94.3%)	37 (80.4%)	
		n = 84	n = 80			n = 84	n = 80	
≥ 75	Suggestions	15 (17.9%)	32 (40.0%)	<0.05	Changes	12 (14.3%)	28 (35.0%)	< 0.05
	No Suggestions	69 (82.1%)	48 (60.0%)		No Changes	72 (85.7%)	52 (65.0%)	

n: number of patients
The data, derived from patients with polypharmacy (six or more medications at admission), are expressed as the number of patients with percentages in parentheses.
†Please note the total numbers of medications changed for these patients were 18 and 50, respectively; they are further analyzed as shown in Tables 4 and 5.

Table 4. The Reasons for the Discontinuation of Medications for Patients with Six or More Medications at Admission

All	Age < 65		Age 65-74		Age ≥ 75		Total	
	Before	After	Before	After	Before	After	Before	After
Duplication†	3	2	1	3	10	9	14	14
No symptoms‡	0	2	0	2	0	14	0	18
Adverse symptoms§	0	1	0	0	2	2	2	3
Drug-disease interactions¶	0	1	0	0	0	0	0	1
Inappropriate dosage[a]	0	0	0	1	0	4	0	5
Drug–drug interactions[b]	0	0	0	1	0	0	0	1
No indications[c]	0	0	0	0	0	2	0	2
Not effective[d]	0	1	0	0	1	0	1	1
Non-adherence[e]	0	0	0	5	1	0	1	5
Total	3	7	1	12	14	31	18	50

†There is an unnecessary duplication with other medications.
‡There are medications prescribed despite the absence of symptoms.
§There are adverse symptoms or signs.
¶There are clinically important drug–disease/condition interactions.
[a]The dosage is not appropriate.
[b]There are clinically important drug–drug interactions.
[c]There is no indication for the medication.
[d]The medication is not effective for the condition.
[e]The medication adherence is not good.

Reasons for the Discontinuation of Medications Table 4 summarizes the reasons for the discontinuation of medications. The total number of cases in which medications were prescribed despite the absence of symptoms ("no symptoms") increased with the use of the checklist (0 prior to the checklist vs. 18 during the use of the checklist). The number of medication discontinuation cases due to "no symptoms" increased in all age groups after the introduction of the checklist. In addition, the number of cases of medication discontinuation for inappropriate dosage and non-adherence increased upon the introduction of the checklist.

The medications discontinued upon the introduction of the checklist were diverse; the most commonly discontinued medications were peptic ulcer medications, antihistamines, and antitussives (Table 5).

DISCUSSION

Our study demonstrated that introducing a checklist to support the appropriate use of multiple medications increased pharmacist intervention and improved appropriate medication prescription. The increase in the total number of pharmacist suggestions for prescriptions and the subsequent changes made to prescriptions by doctors were remarkable.

In this study, we compared the results of interventions in prescriptions by pharmacists among three age groups. We observed a significant increase in prescription suggestions and changes for patients aged ≥ 75 years after introducing the checklist. However, the number of suggestions for and changes in prescriptions also increased for patients aged under 75 years. This observation suggests that up to 20% of patients younger than 75 years are at risk of being prescribed potentially inappropriate medications. Our checklist was useful in

Table 5. Medicinal Group of Reduced Medications Before and After Implementing the Checklist

Medicinal group	Before	After
Peptic ulcer agents	3	8
H2-receptor antagonists	1	1
Proton pump inhibitors	1	3
Other drugs for peptic ulcer	1	4
Antihistamines	1	7
Antitussives	0	5
Vitamins	4	4
NSAIDs	1	3
Antihypertensives	1	3
Blood glucose-lowering drugs	3	2
Laxatives	0	2
Antiemetics	0	2
Others	5	14
Total	18	50

NSAID, non-steroidal anti-inflammatory drug

detecting these cases among younger patients, not just among elderly patients. The data of patients younger than 75 years may not have reached statistical significance in this study because the number of patients with six or more medications among these groups was too small. However, a proportion of patients with polypharmacy is under 65 years of age.[22] In fact, one-fifth to one-quarter of all patients in our hospital taking more than six medications are under 65 years of age. With age, the average number of medications increases;[22] thus, we consider early interventions for younger patients essential to prevent the prescription of unnecessary medications and prevent polypharmacy later in their life. However, based on the total number of medications prescribed before and after implementing the checklist, it appears that intervention by pharmacists had a limited effect on the number of medications at discharge. The number of medications per patient used to treat the disease for which the patient was admitted often increased, especially for patients with cerebral infarction, Parkinson's disease, collagen disease, or diabetes. There was no difference in the purposes of admissions of the patients between before and after using the checklist, and there was no difference in the number of additional medications due to treatment before and after using the checklist. The small decrease in the number of medications at discharge after using the checklist might be due to the intervention.

The most common reason for the discontinuation of medications was "no symptoms." An audit using this checklist revealed many unnecessary medications that had been prescribed despite the absence of symptoms. One possible reason for this is that elderly patients may not understand the purpose of medications and tend to continue a medication even after it is no longer necessary. The major medications discontinued were peptic ulcer medications, antihistamines, and antitussives. These medications had been appropriately prescribed in the first instance, but then continued to be prescribed despite the absence of symptoms.

These data suggest that our checklist was effective in identifying inappropriate prescriptions. Several reports have shown that intervention by pharmacists can reduce inappropriate prescriptions, drug adverse effects, and drug-related hospitalization rates. Our previous effort to standardize lamotrigine audit reduced inappropriate prescriptions; however, it was a standard intervention practice limited to one medication.[23] Gillespie *et al*. reported that ward-based pharmacist intervention reduced emergency department visits and drug-related readmissions for patients over the age of 80 years.[24] Hassan *et al*. reported that a renal drug-dosing service by pharmacists for patients hospitalized with chronic kidney disease increased the proportion of drug dosing that was adjusted taking renal function into account and helped prevent adverse drug events.[25] Although our study has limitations, such as the small number of patients and the lack of a comprehensive evaluation of patients' conditions, it could raise awareness of the importance of pharmacist intervention for controlling the appropriateness of prescribed medications.

Conflict of interest The authors declare no conflict of interest.

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